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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Kathleen A Tyrrell
Liicata & Tryrell P C
66 E Main Street
Marlton, NJ 08053

EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/705,500	Recipon et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above, claim(s) *7-11, 13, and 14* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6 and 12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of Group I, drawn to methods of diagnosing and monitoring cancer in a patient comprising assaying for Lng108, and methods of identifying potential agents useful in the imaging of cancer comprising assaying for molecules which bind to Lng108. The traversal is on the grounds that the restriction is improper as the examiner has not demonstrated undue burden in the search of all pending claims. Applicant argues that all the claims are drawn to the determination of Lng108 and therefore a proper search for any one group would be co-extensive for all remaining groups. This has been considered but not found persuasive. Group III is drawn to a method for inducing an immune response comprising the delivery of Lng108 as a vaccine. Group II is drawn to a method for treating cancer comprising administering an antibody which binds to Lng108 or an agent which decreases the expression or activity of Lng108. Neither group II or Group III are drawn to methods comprising the determination or quantitation of Lng108. Further, the claims of Groups I, II and III are classified differently, necessitating different searches in the U.S. Patent shoes. Classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group.

For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

2. Claims 1-14 are pending. Claims 7 KKC-11, 13 and 14, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-5, 6 in part, and 12, in part, are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-5, 6 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-5, 6 and 12 are rendered vague and indefinite in the recitation of Lng108. Lng108 is a laboratory designation, the meaning of which is unknown in the art. Amendment of the claims to incorporate a SEQ ID NO is recommended.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5, 6 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1, 2, 3, 4, 5 are drawn to a methods of diagnosing cancer, diagnosing metastatic disease, staging cancer, monitoring cancer, monitoring a change in the stage of cancer and a method of identifying potential therapeutic agents for use in imaging and treating cancer, all methods comprising determining the levels of Lng108 in cells, tissues or bodily fluids of a patient. Claim 12 specifically embodies cancer as lung cancer.

(A)Regarding discrepancies between the sequences contained in the CRF and the specification.

The specification teaches that Lng108 and the nucleotides encoding it, are the same as staniocalcin and staniocalcin precursor. However, a comparison of the sequences of SEQ ID NO:1 or SEQ ID NO:2 with the nucleotides encoding staniocalcin or staniocalcin precursor show this not to be the case. For instance, a comparison of SEQ ID NO:2 or the instant invention with Genbank accession number HSU25997 show numerous mismatches and deletions. Further, the instant SEQ ID NO:2 contains large area of ambiguity in the form of residues indicated by "N", and this is insufficient written description to support claims for the detection of Lng108 or the

detection of SEQ ID NO:2. Further, a search for SEQ ID NO:1 hit on staniocalcin precursor but did not "hit" on staniocalcin. In addition , the specification teaches that the primer of SEQ ID NO:5 was used to amplify expressed polynucleotides in tissue samples taken from patients. However, SEQ ID NO:5 would not hybridize to the polynucleotide encoding staniocalcin precursor as said precursor has a run of six "Cs" and the primer has a run of five "Cs". Therefore, one of skill in the art would be subject to undue experimentation in determining if the claims are drawn to the detection of Lng108 as encoded by SEQ ID NO:1 or the detection of Lng108 as encoded by the nucleotides encoding staniocalcin.

(B)As drawn to the detection and monitoring of cancer, the detection of metastatic disease and the staging of cancer and the detection of changes in staging.

The specification teaches the amplification of the polynucleotides SEQ ID NO:1 or 2 by the primers of SEQ ID NO:4 and 5 in tumor tissue and matching normal adjacent tissue. The specification concludes from the data presented in Table 2 that Lng108 is overexpressed in 14 out of 21 lung cancer tissues. However, upon examination of Table 2 it is noted that in 5 out of the 18 primary lung cancers, the amplified polynucleotide was markedly elevated in the normal adjacent tissue relative to the tumor tissue and that in 3 out of the 18 primary lung cancers the levels of amplified polynucleotide were not significantly different in adjacent normal tissue versus in the tumor tissue. The examiner contends that in only 10 out of 18 samples of the primary lung cancer was the amplified polynucleotide elevated in contrast to the adjacent normal tissue and in two of these cases (Lung 16 and 17 it is not known what significance can be attributed to the difference as a standard deviation was not reported. Table 2 further indicates that in other primary tumors such as bladder, kidney, stomach, uterus and two prostate samples, the normal adjacent tissue exhibits a higher level of the amplified polynucleotide that the tumor tissue in seven cases and in two cases it is the same (Endometrium 2, Pancreas 1). One of skill in the art would not know how to use the instant methods for the diagnosis of cancer if normal tissue can exhibit higher values than tumor tissue for the amplified polynucleotide. Further, the specification provides no support as to the staging of cancer or the monitoring of a change in the stage of cancer as the specification does not link the data presented in Table 2 with a stage of cancer.

Claims 2 and 4 are drawn to the diagnosis and monitoring of metastatic cancer. Table 2 provides two samples of secondary bone, renal and metastatic melanoma. The absolute level of amplified polynucleotide varies widely between the samples and again, in one out of the three samples the level of the amplified polynucleotides was three times as high in the adjacent tissues as in the tumor tissues. The specification provides no guidance on the interpretation of a result where normal tissue exhibits the amplified polynucleotides at a level which is three times the level found in the tumor tissue. The specification does not teach if the lung tumor samples would still express the amplified polynucleotide on metastasis to other organs such as liver or bone. The specification dos not teach that the primary bone, renal and melanoma cells expressed the amplified polynucleotides before metastasis to the lung or that there was an increase in expression of the amplified polynucleotides only when the bone, renal and melanoma cells reached the environment of the lung. Given the unreliability of the art, and the lack of teachings in the specification, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to diagnose or monitor metastatic cancer.

(C)As drawn to a method of identifying agents useful in the imaging of cancer.

Claim 6 is drawn to a method of identifying therapeutic agents for use in imaging of cancer comprising the screening of molecules for an ability to bind to Lng108. The specification provides no evidence that the protein expressed from the polynucleotides encoding Lng108 would be present to an extent commensurate with a cancerous state. The specification is not enabling for a method of detecting cancer, staging cancer or detecting metastatic disease comprising detecting polynucleotides for the reasons set forth above. Further, in the event that the specification were enabling for the detection of cancer by means of detecting the instant amplified polynucleotide, it is recognized in the art that an expressed polynucleotide level cannot be relied upon as a surrogate for level of the corresponding protein as a multitude of homeostatic factors control the level of protein expression beyond the level of mRNA transcription. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the

availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus these references teach that expressed polynucleotide levels cannot be relied upon to predict levels of the corresponding proteins. Therefore, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to use the compounds which bind to Lng108 protein in the diagnosis of cancer.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
February 10, 2002